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EXAMINER	
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ART UNIT	PAPER NUMBER
1644	11

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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 4/16/01

☑ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 13-24 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☑ Claim(s) 13-24 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413

DETAILED ACTION

1. Applicant's amendment, filed 4/16/01 (Paper No. 10), is acknowledged.
Claim 13 has been amended.

Claims 13-24 are pending and being acted upon as they read on the PSMA.

Claims 1-12 have been canceled previously.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to applicant's arguments, filed 4/16/01 (Paper No. 10).
The rejections of record can be found in the previous Office Action (Paper No. 7).

3. Claims 13 and 17-24 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to methods of eliciting antitumor responses to prostate tumors by administering:
A) "at least one antigen over represented in the prostate gland or an immunologically effective portion thereof";
B) "nucleic acid that generate said antigen or antigens in situ".

Such "over represented antigens" and "nucleic acid sequences" do not meet the written description provision of 35 USC 112, first paragraph. There is insufficient guidance and direction as to the written description of these "over represented antigens" and "nucleic acid sequences.

Applicant's arguments, filed 4/16/01 (Paper No. 10), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant asserts that the written description as filed is presumed to be adequate unless or until sufficient evidence or reasoning to the contrary has been presented to rebut the presumption.

Appellant acknowledges that applicant should provide a description of sufficient, relevant identifying characteristics so long as a person skilled in the would recognize that the inventor had possession of the claimed invention.

In contrast to applicant's reliance on the disclosure of PSA, PSMA and PAP; the claims are not limited to PSA, PSMA or PAP.

In contrast to applicant's reliance on disclosing methods of preparing immunologically reactive portions assertions; there is insufficient disclosure of the relevant identifying characteristics of overrepresented antigens in the prostate other than PSA, PSMA and PAP or immunologically effective portions thereof, including those claimed immunologically effective portions thereof of PSA, PSMA, and PAP which would elicit an effective antitumor response to prostate tumors in subjects.

In contrast to applicant's reliance on the description of nucleic acids on pages 6-7 and pages 16-17 of the specification; there does not appear to be any written description of a nucleic acid or an amino acid in the application as filed

Applicant asserts that the nucleic acids of the antigens are not required because the nucleic acids sequences of the antigens are not claimed; however the claims recite "wherein said active ingredient comprises a nucleic acid that generates said antigen or antigens in situ".

Applicant directs written support for the nucleic acid sequence of PSMA, PAP and PSA on pages 8-9 of the specification; but applicant does not provide for the written description of the nucleic acids encoding these particular prostate antigens in the specification as filed.

The following of record is reiterated for applicant's convenience.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides (proteins) and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Thus, the specification fails to describe these DNA sequences. The Court further elaborated that generic statements are not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. Finally, the Court indicated that while applicants are not required to disclose every species encompassed within a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, defined by nucleotide sequence, falling within the scope of the genus, See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Therefore, there is insufficient written description for "at least one antigen over represented in the prostate gland or an immunologically effective portion thereof" and "nucleic acid that generate said antigen or antigens in situ". other than that disclosed in the specification as filed under the written description provision of 35 USC 112, first paragraph.

Applicant's arguments are not found persuasive.

4. Claims 13-24 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "full-length PSA, PSMA and PAP"; does not reasonably provide enablement for any "over represented prostate specific antigen" and "immunologically effective portion thereof". The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention commensurate in scope with these claims.

Applicant's arguments in conjunction with Exhibit B, filed 4/16/01 (Paper Nos. 9/10), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant argues that the specification (e.g. pages 6-7, 10, 12, 16) teaches the skilled artisan how to make, formulate and administer full length antigens, immunologically reactive proteins thereof, and nucleic acids encoding one or more of those antigens in situ.

Applicant argues that the claimed methods are not unpredictable because the claimed methods have been show to elicit an immune response in humans; documents cited in the Office Action demonstrate the efficacy of the claimed methods; and the examiner states that the skilled artisan would have a reason to believe the claimed methods are not unpredictable.

Applicant argues in conjunction with Exhibit B that the success of the claimed methods with PSA predicts a similar efficacy with PSMA and PAP and immunologically reactive portions of the antigens and nucleic acid that generates one or more of the antigens in situ.

In citing certain passages; applicant asserts that the Spitler (Cancer Biotherapy 10: 1-3, 1995) and Hodge et al. Int. J. Cancer 63: 231-237, 1995) demonstrate the claimed methods are credible and not unpredictable when read in their entirety.

Applicant relies upon the prior art rejection set forth in the previous Office Action to support the enablement of the claimed methods.

Applicant argues in conjunction with In re Wands that the specification teaches all of the required steps for practicing the claimed methods and that any experimentation required for practicing the claimed methods would not be undue.

The following of record is reiterated herein for applicant's convenience.

Applicant has not provided sufficient biochemical information (e.g. molecular weight, amino acid composition, N-terminal sequence, etc.) that distinctly identifies "over represented prostate antigens" other than "PSA, PAP or PSMA". While "over represented prostate antigen" and "immunologically effective portion thereof" may have some notion of the claimed active ingredients; there is insufficient direction and guidance which enables the skilled artisan to make and use "over represented prostate specific antigen"

and "immunologically effective portion thereof", commensurate in scope with the claimed invention.

Appellant has not disclosed how to use the claimed vaccines and methods to treat prostatic cancer as a therapeutic regimen in humans. There is insufficient evidence of the invention with respect to the in vivo operability of the claimed prostate-specific proteins, peptides or fragments thereof as well as anti-idiotypic antibodies to use appellant's invention.

In vitro and animal model studies have not correlated well with in vivo clinical trial results in patients. Concerning vaccines to elicit antitumor responses in general, the antigenic or immunogenic nature of a protein or an anti-idiotypic antibody does not necessarily correlate with its ability to confer antitumor responses.

As disclosed on page 2, paragraph 1 of the instant specification; applicant discloses that prostate cancer continues to be refractory to treatment despite many years of efforts to improve therapy. Similarly, appellant discloses that at the time the invention was made; vaccine development has been slow and no vaccine approved by the FDA for marketing currently exists for any form of cancer.

Appellant has not provided sufficient objective evidence that predicts the efficacy of the instant invention drawn to "over represented prostate antigens" or" immunologically active portions of PSA, PSMA or PAP" in the specification as filed or a portion thereof for the treatment or prevention of human prostatic cancer.

As the instant inventor acknowledges (Spitler, Cancer Biotherapy 10:1-3, 1995; page 1, column 1, paragraph 1; 1449); "Ask practicing oncologists what they think about cancer vaccines and you're likely to get the following response: "cancer vaccines don't work". Ask a venture capitalist or the director of product development at a large pharmaceutical company, and you're likely to get the same response". Therefore, applicant has recognized the lack of predictability of the nature of the art and state of the prior art to which the instant invention pertains, as similarly disclosed on page 2 of the specification. Also, such disclosures clearly indicate that the amount of direction or guidance presented in the specification is limited, and would not permit a person skilled in the art to use the invention without undue experimentation at the time the invention was made.

Furthermore, Hodge et al. (Int. J. Cancer 63: 231-237, 1995; 1449) discloses that previous attempts to actively immunize patients with prostate adenocarcinoma cells admixed with adjuvant shown little or no therapeutic benefit (page 231, column 1, first paragraph of Introduction). Here, the reference discloses that these previous attempts to actively immunize were known in 1990, prior to appellant's invention. Such prostate adenocarcinoma cells and normal prostate cells express common antigens. Therefore, targeting prostate-specific antigens that are expressed on both normal and tumor cells in cancer immunotherapy to target tissue-specific antigens was known and practiced at the time the invention was made.

With respect to prostate-specific immunotherapy, Hodge et al. (Int. J. Cancer, 1995; 1449) discloses that previous attempts to actively immunize patients with prostate adenocarcinoma cells admixed with adjuvant shown little or no therapeutic benefit (page 231, column 1, first paragraph of Introduction). Models of evaluation of prostate therapeutics including the canine and the Dunning rat are not practical for PSA-recombinant vaccines due to the very low homology of rat and canine PSA to human PSA (page 231, column 2, paragraph 2). The fact that human PSA is a secreted antigen should be taken into consideration for its potential use as a target for human prostate cancer, as the secreted antigen may also reduce immunoglobulin responses by forming antigen-antibody complexes and/or potentially anergizing specific T cell responses (page 235, column 1, lines 1-6). An immune reaction directed against PSA could lead to side effects resulting from cross-reactivity with other kallikrein family members (page 235, column 2, lines 4-6). Therefore, the use of prostate-specific antigens in vaccines are likely to be limited by either neutralization by secreted prostate antigen or by inducing autoimmunity. Although the recombinant human PSA construct was unable to elicit an anti-PSA IgG response, PSA-specific IgM response were noted in all immunized monkeys (page 236, column 1, paragraph 1). However, these antibody responses were of low titer, were short-lived and could not be boosted. It is noted that the monkeys developed in vitro lymphoproliferative responses to PSA (page 236, column 1, paragraph 2). However, it is not clear that such studies can be extrapolated to humans because in the difference in MHC motifs between rhesus and humans and the levels of expression of class I and II MHC on rhesus vs. human prostate and human normal prostate vs. prostate carcinoma (page 236, column 2, last paragraph). In addition to these cautions with respect to appropriate antigen presentation and subsequent immune responses (issue of MHC), this reference clearly indicates limited antibody responses and only some level in vitro cellular immunity with prostate specific antigen immunization. Also, this reference clearly indicates the limitations of animal models in prostate cancer modalities and that previous attempts at human prostate cancer vaccination with whole cells.

Full enablement of claims on vaccines should include teachings on the relevant immunogenic proteins and portions thereof, the level of neutralizing antibody or cellular immunity produced and the efficacy of the vaccine against subsequent inoculations of the intended pathogen, in this case a prostate tumor. Since the immune response is considered to be one of the most complex and unpredictable biological processes, without any guidance or teachings of any of the above, it is considered that it would require undue experimentation for the ordinary skilled artisan to make or to use the invention as claimed.

With respect to "immunologically effective portion thereof", the instant claims are not enabled for the breadth of "immunologically effective portion thereof". The characteristics of these antigens or portions are not clearly defined and encompasses potentially thousands of different polypeptides and peptides. The specification fails to provide sufficient guidance as to how to determine all such polypeptides and peptides. It would require undue experimentation to produce all such possible polypeptides and peptides without more explicit guidance from the disclosure.

The goal of tumor vaccination is the induction of tumor immunity to prevent tumor recurrence and to eliminate residual disease. Ezzell reviews the current thinking in cancer vaccines and states that tumor immunologists are reluctant to place bets on which cancer vaccine approach will prove effective in the long run (J. NIH Research 7: 46-49, 1995; see entire document, particularly the last paragraph; 1449). It has been well known in the art that tumor cells in vivo simply do not display their unique antigens in ways that are easily recognized by cytotoxic T lymphocytes (Ezzell; page 48, column 2, paragraph 2). Furthermore, no one is very optimistic that a single peptide or a virus carrying the gene encoding that peptide will trigger an immune response strong enough to eradicate tumors or even to prevent the later growth of micrometastases among patients whose tumors have been surgically removed or killed by radiation or chemotherapy (Ezzell; page 48, paragraph 6).

With respect to inducing prostate tumor-specific cytotoxic T lymphocytes; Peshwa et al. (The Prostate 36: 129-138, 1998) discloses that the protein sequence of PAP was evaluated using an algorithm to detect contiguous 9-amino acid peptides stretches which could potentially bind the HLA-A2 molecule; that various binding affinities were noted among the tested peptides, resulting in PAP-5 epitope as the most relevant for PAP-based therapeutic vaccines for prostate cancer (see Results); and that of the five nonapeptides shown to exhibit strong binding affinity for the HLA-A2 molecules, only PAP-5 is contained with the mature secreted PAP protein (page 136, column 1, paragraph 1).

While page 12 of the specification discloses screening for identifying peptides which may be important epitopes; applicant has not provided sufficient direction and guidance nor objective evidence in identifying or identification with "immunologically effective portions" of "over represented prostate antigens, including PSA, PSMA, PAP".

While Peshwa et al. (The Prostate, 1998) discloses that similar approaches employing dendritic cells loaded with HLA-A2 binding peptides of PSMA have been reported to have a clinical benefit (see Discussion); it appears that undue experimentation would be required of one skilled in the art to practice the claimed methods and compositions in providing effective vaccines for prostatic cancer using the teaching of the specification alone.

Insufficient direction or guidance is provided to assist one skilled in the art in the selection of all such possible "over represented antigens" and/or "immunologically active portions thereof, including PSA, PSMA and PAP" nor is there sufficient objective evidence provided that all such "antigens" and "immunologically active portions thereof" would be effective to stimulate antitumor responses .

The specification dos not provide a sufficient enabling description of the claimed invention. There is insufficient direction and guidance to enable a skilled artisans to make and use "over represented antigens" and/or "immunologically active portions thereof", as recited in the claims. A person of skill in the art would not know which "over represented antigens" or "immunologically active portions of said over represented antigens, including PSA, PAP, and PSMA" are essential or effective to stimulate antitumor responses, which "antigens"/"portions thereof" are non-essential or noneffective, and what particular lengths identify essential or effective portions. The problem of predicting polypeptide structure from mere sequence data of limited full length prostate antigens sequences and, in turn, utilizing predicted structural determinations to ascertain immunologically active portions of over represented prostate antigens and finally what changes can be tolerated with respect thereto and, in turn, which stimulate antitumor responses is complex and well outside the realm of routine experimentation

In view of the lack of predictability of the art to which the invention pertains and the lack of established clinical protocols for effective cancer vaccines and prostate cancer therapies; undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for establishing protective antitumor responses.

7. With respect to claims drawn to nucleic acids that generate prostate antigens; the following is noted.

The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See In re Hawkins, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); In re Hawkins, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and In re Hawkins, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

An application as filed must be complete in itself in order to comply with 35 U.S.C. 112; however this does not bar incorporation by reference. Ex parte Schwarze, 151 USPQ 426 (Bd. of Appeals, 1966). an application for a patent when filed may incorporate "essential material" by reference to (1) a United States patent or (2) an allowed U.S. application, subject to the conditions set forth below. "Essential material" is defined as that which is necessary to (1) support the claims, or (2) for adequate disclosure of the invention (35 U.S.C. 112). "Essential material" may not be incorporated by reference to (1) patents or applications published by foreign countries or regional patent offices, to (2) non-patent publications, to (3) a U.S. patent or application which itself incorporates "essential material" by reference or to (4) a foreign application. See In re Fouche, 169 USPQ 429; 439 F.2d 1237 (CCPA 1971).

Nonessential subject matter may be incorporated by reference to (1) patents or application published by the United states or foreign countries or regional patent offices, (2) prior filed, commonly owned U.S. applications or (3) non-patent publications, for purposes of indicating the background of the invention or illustrating the state of the art.

The referencing application must include (1) an abstract, (2) a brief summary of the invention, (3) an identification of the referenced patent or application, (4) at least one view in the drawing in those applications admitting of a drawing, and (5) one or more claims. Particular attention should be directed to specific portions of the referenced patent or application.

As indicated above in Sections 5/6; the nucleic acids of PSA, PSMA and PAP are essential to the claimed invention. Applicant is invited to consider incorporating by reference the key nucleic acids encoding PSA, PSMA and PAP, provided there is sufficient direction and particularity of said nucleic acids in the specification as filed and providing the appropriate Hawkins Declaration. See Illustrative Antigens on pages 7-10 of the specification as filed.

8. Claim 24 stands rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. The specification as originally filed does not provide support for the invention as now claimed: "wherein said subject is afflicted with metastatic prostate and/or where said subject has been surgically treated to excise said tumor but is at risk for recurrence".

Applicant's arguments, filed 4/16/01 (Paper No. 10), have been fully considered but are not found convincing essentially for the reasons of record.

Appliant argues the claimed subject matter need not be described literally in order for the disclosure to satisfy the written description requirement.

Applicant relies upon pages 4-5 and 17-19 for the written description of the claimed subject matter

However these sections of the specification as filed do not appear to provide for the written description of the claimed methods : "wherein said subject is afflicted with metastatic prostate and/or where said subject has been surgically treated to excise said tumor but is at risk for recurrence".

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention and that the invention, in that context, is whatever is now claimed.. See MPEP 2163.02. Also, the failure to meet the written description requirement under 35 USC 112, first paragraph arises when the claims are changed after the filing date to change the scope of the disclosure, which does encompass setting forth subgeneric claims (see MPEP 2163.05).

The specification does not provide sufficient blazemarks nor direction for the instant methods encompassing the above-mentioned "limitations" as they are currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office action
Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above.
Also, see MPEP 714.02 and 2163.06

Applicant's arguments are not found persuasive.

5. Upon reconsideration of applicant's arguments, filed 4/16/01 (Paper No. 10), which rely upon the definition set forth on page 5 of the specification, the previous rejection under 35 U.S.C. § 112, second paragraph, with respect to "over represented antigens", has been withdrawn.

6. Claims 13-24 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Spitler (U.S. Patent No. 5,738,867 in view of Israeli et al. (U.S. Patent No. 5,538,866) and in view of art acknowledged methods of delivering antigens of interest to stimulate antitumor responses, as disclosed on pages 10-19 of the instant specification.

Applicant's arguments, filed 4/16/01 (Paper No. 10), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant argues that the prior art provides neither the suggestion nor the motivation of eliciting an immune response against host prostate antigens;
however Spitler teaches methods of delivering antitumor vaccines with tumor associated antigens, including prostate antigens (see Summary of the Invention), as well as known methods of delivering said tumor associated antigens to stimulate antitumor responses, encompassed by the claimed invention (see entire document);
Israeli et al. teach PSMA , including nucleic acids and methods of expressing said PSMA, as well as its expression on prostate tumors (see entire document, including Background of the Invention and Detailed Description of the Invention) as well as highly immunogenic domains of PSMA (e.g. column 3, paragraph 1) and
Pages 10-19 of the specification discloses the art known methods of delivering antigens, including tumor associated antigens, of interest to stimulate antitumor responses encompassed by the claimed methods.

Given the teachings of Israeli et al. that PSMA is useful as a marker for prostate cancer; one of ordinary skill in the art at the time the invention was made would have been motivated to substitute the prostate tumor associated antigen PSMA into the methods of stimulating antitumor responses, as known and practiced in the prior art, as taught by Spitler and acknowledged by the specification as to treat prostate cancer. It would have been obvious to the ordinary artisan to use PSMA in patients with metastatic prostate tumors and/or patients who have had the prostate tumor removed surgically to elicit antitumor responses in order to treat said cancer patients. Also, it would have been obvious to the ordinary artisan to select portions, particularly extracellular portions of PSMA to stimulate antitumor responses. From the teachings of the references and known in the prior art; it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

7. Claims 13-24 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 5,925,362. Although the conflicting claims are not identical, they are not patentably distinct from each other because the patented claims are a species of instant methods.

Applicant's amendment, filed 4/16/01 (Paper No. 10), request that this rejection be held in abeyance until the above-identified issues have been resolved.

8. No claim is allowed.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

PHILLIP GAMBEL

Phillip Gambel, PhD.
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June 26, 2001